Nutrients and degenerative eye diseases

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Cataract (opacity of the lens) and age-related degeneration of the macula of the retina are very common causes of disability in old age, and people are living longer. It seems likely that both of these conditions result from gradual photo-oxidative damage. The proteins in cataractous lenses are oxidized and 50 per cent of the fatty acids in membranes of retinal photo-receptors are highly polyunsaturated. The eye normally has unusually high concentrations of vitamin C and zinc which could have protective functions against free radical damage. For cataracts five reported case-control studies are reviewed and two prospective studies one of which included a very large number of subjects. Vitamin intakes were estimated from dietary histories or blood levels. In five of the six studies in which vitamin C was measured it appeared to be protective and vitamin E and carotenoids appeared protective in 5/7 studies. Other descriptive epidemiological studies are going on, including one in the Blue Mountains near Sydney. It is concluded that controlled trials of antioxidant nutrients for cataract prevention are now warranted. As to age-related mucular degeneration (ARMD), severe vitamin E deficiency is known to cause (a different type of) retinal degeneration spontanously in humans (with cystic fibrosis or abetalipoproteinaemia) and experimentally in animals. Only three human case-control studies of ARMD and diet have been reported thus far and no clear relationship with any particular nutrient has emerged yet. Supplements containing antioxidant vitamins and zinc are being advertised and used in the USA and elsewhere but this is ahead of the evidence. More observational studies are needed and the US National Eye Institute is planning a 10 year intervention study, known as AREDS (Age-Related Eye Disease Study).

Age-related degeneration of the macula of the retina (the reading centre at the back of the eye) and cataract (opacity of the lens) toward the front of the eye are important causes of disability in older people. They account together for approximately 60 per cent of all diagnoses for people over 50 years of age attending the Royal Blind Society of NSW in the years 1984–89[1]. Age-related macular degeneration was responsible for 55% of blindness registrations in 1988[2]. As the life expectancy of our community is gradually extended we want those extra years of life to be worth living. Enjoyment of life and mobility are very much reduced if an old person cannot read, watch television or see where they are walking.

In a random sample of 387 old people in Newcastle, NSW of average age 75 years examined by Mitchell and Darzins in 1990 and 1992, 34 per cent had present cataract or had had a cataract extracted; 8 per cent had advanced age-related macular degeneration (AMD) and a further 32 per cent had early AMD[3].

There is some evidence suggesting that exposure to sunlight is a causative factor for both cataract and macular degeneration. Ultraviolet irradiation is probably increasing in Australia with the thinning of the ozone layer. Cataract is more prevalent in people with occupational exposure to sunlight[4] and in tropical countries[5]. The evidence, however, for a sunlight-AMD association is less strong. The Chesapeake Bay (US) Watermen study found a weak association between advanced AMD and sunlight exposure[6]. A large case-control study in Newcastle, NSW, however, found no significant sunlight-AMD link[7].

Age-related macular degeneration appears to have increased in Newcastle, NSW between 1962 and 1987; throughout this 25 year period a single ophthalmologist was the sole arbiter for the blind pension in the region. AMD accounted for 26 per cent of blind registrations in the early part of this period and 40 per cent for the last 10 years[3].

Nutrition researchers have given a lot of attention to diet and dental caries, coronary heart disease and even some types of cancer but for most of us the hypothesis that habitual diet may be a determinant of degenerative eye diseases is only now appearing on the horizon. Yet we should have suspected this from the unusual concentration of some nutrients in the eye. The lens and aqueous humour normally contain 40 times the vitamin C concentration of plasma. The first described function of vitamin A is in the rods and cones of the retina and the most severe effect of vitamin A deficiency is seen in the cornea. The choroid has the highest zinc concentration of all tissues in the body. The retina also concentrates vitamin C.

Cataracts

The lens of the eye consists of 63 per cent water and 35 per cent proteins, nearly all of which are highly specialized, normally transparent and turn over extremely slowly[8]. On examination with the slit lamp, opacities in the lens are classified by the region affected as cortical, nuclear, posterior subcapsular or mixed and by severity. The causative factors may be different for opacities at these different sites. Posterior subcapsular is the least common site and is often associated with diabetes and corticosteroid therapy[6,9].

Factors to date associated with the common nuclear and cortical cataracts include:

Age
Female gender[6,9]
Diabetes mellitus
Corticosteroid therapy
Sunlight[10]
Oxygen (hyperbaric oxygen therapy)[11]
Smoking[12]
Family history
Brown iris colour[10]
Lower socio-economic and educational status[6,9].

The most satisfactory hypothesis for the pathogenesis of cataract is that it results from photochemical oxidative alteration of the lens crystallin proteins. Proteins in cataractous lenses are indeed extensively oxidized; exposure to pure oxygen accelerates cataract production in mice; the antioxidant BHT prevents development of cataracts in rats fed 50 per cent galactose. The three major antioxidants in the lens are ascorbate (vitamin C), tocopherol (vitamin E) and glutathione.

Evidence for a protective effect of vitamin C includes the reduction of vitamin C concentration in cataractous lenses. The nucleus, where most cataracts occur contains less vitamin C than the rest of the lens; in lens culture experiments vitamin C protects against damage from UV light[8]. The other antioxidant, vitamin E greatly delays the onset of cataracts in Emory mice (which usually develop cataract between 6 and 12 months of age)[13].

The human epidemiological evidence about nutrients and cataract comes mostly from case-control studies, with two cohort studies. A number of other studies are presently underway. Jacques et al.[14] report a case-control of 77 patients with (cortical) cataract and 35 matched controls, all under 70 years of age in Boston. Nutritional status was estimated in a masked manner by blood levels of nutrients. In this small study, vitamin D, total carotenoids and vitamin C appeared to be protective. In a subsequent paper[15] vitamin C intake was reported protective (statistically significant) and so was vitamin E intake (not significant).

In a more recent and larger case-control study in Boston[16], with 446 patients (40–79 years) and a similar number of controls, nutrient intake was estimated by a standard food frequency questionnaire. Intake of vitamin C was protective for cataracts at all sites, especially nuclear. Intakes of vitamin E, riboflavin and vitamin A were protective but not for posterior subcapsular opacities. Presumably vitamin A included carotene intake. The controls had refractive errors or a completely normal eye examination. They were on average 5 years younger and included a higher proportion of men than the cases.

In London, Ontario[17] 175 patients who were awaiting or had just undergone cataract surgery were individually matched for age and sex with the same number of controls, some of whom had mild degrees of lens opacity. The controls were found to use significantly more supplementary vitamins C and E.

Preliminary reports from the Beaver Dam Eye Study[18], a large population-based survey of eye degeneration in people 43–84 years of age in a township in Wisconsin (with photographic standardization of the grading) indicate moderate protective effects of intakes of vitamin E, niacin, zinc and several carotenoids. Results differed between men and women. The negative association of vitamin C intake with cataracts was unimpressive.

In the Nurses' Health Study[19] 121 700 female nurses are being followed. Prior nutrient intakes of those who developed 493 cataracts that were extracted showed a negative association with carotene and vitamin A intake. Dietary vitamins C and E and riboflavin were not associated. Spinach rather than carrots was negatively associated, raising the possibility that the most protective carotenoid(s) may not be β-carotene. Long term use of vitamin C supplements (but not multivitamins) had a significant (protective) odds ratio for cataract surgery of 0.55.

In Finland a case-control study, nested within a cohort study, examined the stored serum of 47 patients admitted to ophthalmological wards for cataract surgery over 15 years and of two controls per patient, individually matched for age, sex and municipality[20]. Low serum α-tocopherol and β-carotene predicted cases of surgical cataract and the predictive power was greater when both were low. Unfortunately serum vitamin C could not be measured in this study.

These authors and others[14] concluded that controlled trials of antioxidant vitamins in cataract prevention are now warranted.

Age-related macular degeneration (AMD)

This condition is more serious than cataract because in most cases, no treatment is available. As with cataract there are different morphological types of AMD. The epidemiology is different: there appears to be no excess in females and no relation to level of education. Hypertension and refractive error (hyperopia) may be associated. Sunlight exposure and blue iris colour may also be associated with AMD.

Feeney and Berman[21] suggested the hypothesis that exposure to UV or visible light can lead to free radical formation. These free radicals may increase with aging and lead to lipid peroxidation of the photoreceptor outer segment membranes of the retina that are very rich in highly polyunsaturated fatty acids – their content of docosahexaenoic acid (22:6 ω-3) is about 50 per cent of total fatty acids[22]. The retina contains vitamin A, whose essential function is well established. The retina and choroid have very high concentrations of vitamin C and the highest zinc concentration of all tissues. Presumably these nutrients are concentrated in and near the sensory retina for a purpose.

In dogs, monkeys and rats vitamin E deficiency causes retinal degeneration[23,24]. In humans, pigmentary degeneration of the peripheral retina is a feature of chronic vitamin E deficiency (as in cystic fibrosis and abetalipoproteinaemia)[25]. Zinc deficiency is associated with night blindness[26] and abnormalities of retinal pigment[27]. Katz et al. studied the effects of antioxidant deficiency (vitamin E and selenium) in albino rats. There were increases in retinal pigment and losses of photoreceptor cells, particularly from the central retina. 'Many of the changes that occur in these ocular tissues as a result of inadequate antioxidant protection are similar to changes that occur more slowly in the eye during normal aging. Thus it seems possible that many of the deleterious changes which occur in the retina and retinal pigment epithelium during aging are a consequence of antioxidative reactions. In some cases these age-related changes may be severe enough to cause a profound loss of sight, as occurs in senile macular degeneration'[28].

Goldberg et al.[29] related nutritional intakes with eye examinations in the NHANES 1 Survey (1971–2) in the USA. Subjects were all under the age of 75 years (so omitting the most vulnerable ages). Intake of vitamin A and of fruits and vegetables rich in vitamin A (and therefore carotenes) were significantly protective but an apparent negative association with vitamin C intake was no longer significant after adjusting for demographic and medical factors. In a much smaller case-control study Blumenkrantz et al.[30] found no association of AMD with serum vitamin A, C or E. However their use of spouses as controls biased against finding any dietary effect.

Sanders et al.[31] could find no difference in plasma concentrations of retinol, five individual carotenoids or α-tocopherol between 65 elderly people with AMD and 65 matched controls in London. Ophthalmological diagnoses were done at Moorfields Hospital. Plasma vitamin Cs were not measured.

Although supplements containing antioxidant vitamins and zinc are being advertised for protection of the aging eye in the USA and worldwide, convincing human evidence for any protective effect of nutrients against AMD is lacking at present. Many more observational studies will be needed and then some intervention trials before the nutritional hypothesis can be established. A 10 year intervention study is being planned by the US National Eye Institute, known as AREDS (Age-Related Eye Disease Study). While subjects are being recruited, at the moment no intervention has yet commenced. At present the only epidemiological data is in three studies.

Recently published data from the Eye Disease Case Control Study[32] found that a decreased risk of neovascular AMD was associated with higher levels of serum carotenoids (sum of lutein/zeaxanthin, β-carotene, α-carotene, cryptoxanthin and lycopene).

It is clear from what has been said that good quality epidemiologic data is urgently needed concerning the prevalence of degenerative eye diseases and their relation to suspected environmental factors including diet. A major study in Australia, known as the Blue Mountains Eye Study, is now nearing completion, and will address this question. The investigators include P. Mitchell, W. Smith, K. Webb and S. Leeder. Data collection should be completed by September, 1993.

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Asia Pacific J Clin Nutr (1993) 2, Suppl 1, 47–50

營養與變性眼疾

摘 要

白內障（晶狀體混濁）和視網膜黃斑變性是老年人和長壽者殘廢的常見原因。這兩種情況似由于逐步光氧化損害所致。白內障晶狀體蛋白被氧化，視網膜的光受體膜內有５０％脂肪酸是高度不飽和的。眼睛通常有高濃度的維生素Ｃ和鋅，對自由基的損害有保護作用。

作者評論了七個白內障的研究報告，從膳食歷史或血液含量來評估維生素進食。在六個研究中，有五個研究認爲維生素Ｃ對白內障有保護作用，在７個研究中，有５個研究認爲維生素Ｅ和胡蘿卜素對白內障有保護作用。其它流行病學的研究，包括一個雪梨市附近藍山市的研究在進行中。從對照實驗推斷，目前已證實抗氧化營養素對白內障有預防作用。

關于與年齡有關的視網膜黃斑變性（ＡＲＭＤ），已知嚴重維生素Ｅ缺乏是引起人類（患有囊性纖維變性或無β－脂蛋白血症）和實驗動物自發的視網膜變性，但到目前爲止，只報導了三個ＡＲＭＤ和膳食的人類對照研究，仍未發現與任何特殊營養素有明顯的關系。在美國及各地已宣傳補充抗氧化維生素和鋅來保護與年齡有關的眼疾，但這都在證實之前。更多的觀察研究是需要的，美國國家眼科研究所正在計劃一個十年研究，名爲ＡＲＥＤＳ（與年齡有關的眼疾研究）。

Contributors

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